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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/004,348	10/18/2001	King Chuen Li	STAN-182	3700

24353 7590 10/18/2004

BOZICEVIC, FIELD & FRANCIS LLP
1900 UNIVERSITY AVE
SUITE 200
EAST PALO ALTO, CA 94303

EXAMINER	
LY, CHEYNE D	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 10/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/004,348	LI ET AL.	
	Examiner	Art Unit	
	Cheyne D Ly	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-7 and 23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-7 and 23* is/are rejected.

7)☒ Claim(s) *23* is/are objected to.

8)☒ Claim(s) *1,4-7 and 23* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' arguments filed July 27, 2004 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

2. The cancellation of claims 2, 3, and 8-22 has been acknowledged.

3. Claims 1, 4-7, and 23, Species: MRI, are examined on the merits.

4. FINAL OFFICE ACTION.

OBJECTION

5. Claim 23 is objected to because of the following informalities: There is a typographical error in the term "ahuman" due to lack of appropriate spacing. Appropriate correction is required.

CLAIM REJECTIONS - 35 U.S.C. § 112, SECOND PARAGRAPH

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1, 4-7, and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. This rejection is maintained with respect to claims 1 and 4-6, as recited in the previous office action mailed January 29, 2004. The instant rejection has been extended to claims 7 and 23.

9. The rejection of claims 7 and 23 has been necessitated by claim amendment.

RESPONSE TO ARGUMENT

10. Applicant argues by pointed to support in the specification [¶ 62] wherein "suitable control tissues include normal cell populations, ...in disease progression." Applicant's argument has been fully considered and found to be unpersuasive because the pointed to support does not resolve the vague and indefinite issue discussed below. It is noted that paragraph 62 discloses "genes over represented in the pathologic cell population relative to a control tissue, e.g. normal cell populations, other regions of the diseased tissue, earlier or later time points in disease progression, etc., represent genes potentially suitable for use as targets of imaging agents." Therefore, the pointed support does not resolve the vague and indefinite issue because claim 1 remains unclear whether the cellular sample which is being compared to a control tissue is cell populations, other regions of the diseased tissue, or earlier or later time points in disease progression.

REJECTION RE-ITERATED

11. Specific to claim 1, line 8; and claim 7, line 11, the limitation of comparing expression in cellular sample with a control tissue causes the claim to be vague and indefinite because it is unclear whether the comparison of gene expression between samples obtained from a tissue and said tissue or between a cellular sample from a tissue to other samples from said tissue. Clarification of the metes and bounds of the claim is required. Claims 4-6 and 23 are rejected for being dependent from claim 1.

CLAIM REJECTIONS - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1, 4-6, and 23 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Schiffenbauer et al. (1997).

14. This rejection is maintained with respect to claims 1 and 4-6, as recited in the previous office action mailed January 29, 2004. The instant rejection has been extended to claim 23.

15. The rejection of claim 23 has been necessitated by claim amendment.

RESPONSE TO ARGUMENT

16. Applicant argues that Schiffenbauer et al. does not disclose a method that requires dynamic contrast MRI. Further, Applicant argues that the "gene expression of Schiffenbauer et al. was therefore performed on cultures of cells grown *in vitro*, which were not directly correlated with the tumors obtained from animals, (which tumors were imaged)." Applicant's arguments have been fully considered and found to be unpersuasive.

17. Schiffenbauer et al. discloses a method requiring *in vivo* MRI wherein vascularization reduced the mean intensity in a region of 1 nm surrounding the spheroid-containing bead relative to a distant tissue (angiogenic contrast, 20)...correlate well with the density of blood vessels determined from skin specimens of the same mice. MRI analysis enabled us to follow each mouse independently and to determine the peak of the angiogenic activity

(dynamic)..." (page 13204, column 1, MRI and NMR studies §). Further, Schiffenbauer et al. discloses visual examination of the skin specimens dissected at the end of the experiment from all mice confirmed the MRI result from tumors in the ovariectomy group versus control group (page 13205, column 1, 28-34). It is noted that the limitation of "dynamic contrast MRI" has not been specifically defined in the instant specification; therefore, the disclosure of Schiffenbauer et al. cited above is consistent with said limitation.

18. Specific to Applicant's argument that the method of Schiffenbauer et al. is performed on cultures of cells grown *in vitro*, which were not directly correlated with the tumors obtained from animals, it is noted that claim 1 recites "*in vivo*" as directed to the imaging step. However, the steps as recited in claim 1, lines 6-11 has not been limited to an "*in vivo*" type of step, because only lines 3-5 recite the steps of "in vivo images. " Therefore, the disclosure of Schiffenbauer et al. for a method comprising in vivo analysis of ovarian cancer tissues via MRI (page 13204, Animal Protocols § and MRI and NMR Studies §; and page 13205, Figure 2) is consistent with the argued limitation. Specific to the steps as recited by lines 6-11, said steps are not limited to the "in vivo" limitation as argued by Applicant. Therefore, the limitation of "in vivo" is not required for anticipation basis are directed to the limitations of claim 1, lines 6-11.

19. Further, claim 1, lines 6-8, recites the step of "obtaining a cellular sample from said diseased tissue"...corresponds to said imaging feature." It is noted that the limitation of "corresponds" has not been specifically defined in the specification. Therefore, said limitation has been interpreted as broadly as reasonable. The limitation of "corresponds" has been reasonably interpreted as "to be similar or equivalent in character, quantity, origin,

structure, or function." Therefore, the disclosure of Schiffenbauer et al. of determining expression of gene or gene products in human epithelial ovarian carcinoma cells by DNA synthesis studies and *in situ* hybridization (page 13205, column 2, lines 1, to page 13206, column 2, lines 13) is consistent with the required limitation of claim 1, lines 6-8 and dependent claims 4 and 5. The prior art citation has been extended to new claim 23.

REJECTION RE-ITERATED

20. Schiffenbauer et al. discloses a method of screening for hormone therapeutics as directed to ovarian cancer (Abstract et al.).

21. The method of Schiffenbauer et al. comprises in vivo analysis of ovarian cancer tissues via MRI and analyzing images for specific features from tissues harvested from nude mice (page 13204, Animal Protocols § and MRI and NMR Studies §; and page 13205, Figure 2). Further, in Situ hybridization is performed on frozen specimens for detection the expression of gene products such as mRNA of diseased tissues versus control wherein the data show induced expression in the gonadotropin-stimulated spheroids (page 13204, Reverse Transcriptase-PCR Analysis §, In Situ Hybridization §, and Figure 5), as in instant claims 1, 4, and 5.

22. OC109 and OC238 human epithelia ovarian carcinoma cells are cultured in DMEM (suspension) (page 13203, Cell Culture §), as in instant claims 6 and 23.

23. Claim 7 is rejected under 35 U.S.C. 102(a) as being clearly anticipated by Munoz et al. (1999).

24. The instant rejection has been necessitated by claim amendments.

25. Munoz et al. discloses a method for screening DRPLA directed to humans using cranial MRI analysis and molecular detection of CAG triplet expansion in the B37 gene on chromosome 12 (Abstract etc.), as in instant claim 7, lines 1-7.

26. Before the genetic tests, MRI images of a human III-7 patient indicates cerebellar and brain stem atrophy and diffuse high intensity signals in T2 weighted images of cerebral white matter and brain stem (page 813, Discussion §, columns 1-2). Genomic DNA was obtained from human III-7 patient (page 811, column 2, Material and Methods §), as in instant claim 7, lines 8-9.

27. The length of CAG repeats in the B-37 of normal patients is generally under 25, whereas patients with DRPLA have a length greater than 49 expansions (upregulated). The correlation between the sized of the expanded alleles and the age at onset and the phenotype has been found (page 813, column 1, lines 50-55), as in instant claim 7, lines 10-13.

CONCLUSION

28. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

29. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

30. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

31. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

32. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

33. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (571) 272-0716. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

34. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (571) 272-0722.

C. Dune Ly
10/13/04

Justin D. Woodward 12/14/04